CONTENTS

Chapter 1 General Introduction 1

Chapter 2 **Synthesis, characterization and biological activity of novel 2-aryl benzimidazole derivatives** 20

- 2.1 Physical Properties of Benzimidazole 22
- 2.2 Chemical Properties of Benzimidazole 23
- 2.3 Functionalization of Benzimidazole Nucleus 23
  - 2.3.1 Direct coupling at the C-2 position 23
  - 2.3.2 Substitution at the N-1 position 23
  - 2.3.3 Cyclization between the N-1 and C-2 position 24
  - 2.3.4 Doebner-Von Miller reaction at the C-7 position 25
- 2.4 Benzimidazole derived metal complexes 26
- 2.5 Synthetic Approach for Benzimidazole Molecules 26
  - 2.5.1 General synthetic methodology 27
  - 2.5.2 Benzimidazole ring closure 27
  - 2.5.3 Diels-Alder reaction 28
  - 2.5.4 Microwave assisted synthesis of benzimidazole 29
  - 2.5.5 Benzimidazole natural products 30
- 2.6 Benzimidazole as a Template for Various Biological Activities 30
  - 2.6.1 Anti-tumor/Anticancer activity/Anti proliferative 30
  - 2.6.2 Antimicrobial activity 41
  - 2.6.3 Anthelmintic activity 44
  - 2.6.4 Antihypertensive activity 46
  - 2.6.5 Antiretroviral activity 47
  - 2.6.6 Antiinflammatory, analgesic and antiulcer activity 49
  - 2.6.7 Opportunistic infections 52
  - 2.6.8 Antioxidant/Radio-protective activity 52
  - 2.6.9 Carbonic anhydrase inhibitors 53
  - 2.6.10 Anticonvulsant and antidepressant activity 54
- 2.7 Current work 55
- 2.8 Reaction Scheme 56
  - 2.8.1 Synthesis of 3-[(3-Amino-4-methylamino-benzoyl)-pyridin-2-yl-amino]-propionic acid ethyl ester (1) and (mpd1) 56
  - 2.8.2 General scheme of novel benzimidazole compounds 58
- 2.9 Reaction Mechanism 59
- 2.10 Experimental 60
- 2.11 Physical data 60
  - 2.11.1 Physical data of novel benzimidazole compounds (mpd 1-12 and BI 1-6) 60
- 2.12 Spectral discussion 61
  - 2.12.1 Mass spectral study 61
  - 2.12.2 IR spectral study 62
  - 2.12.3 1H NMR spectral study 62

2.12.4 Elemental analysis 62
2.12.5 Spectral data of synthesized compounds (mpd 1-12 and BI 1-6) 63
2.12.5.1 1H NMR spectrum of 1 69
2.12.5.2 Carbon NMR spectrum of 1 71
2.12.5.3 DEPT spectrum of 1 71
2.12.5.4 1H NMR spectrum of mpd 1 73
2.12.5.5 1H NMR spectrum of mpd 2 75
2.12.5.6 1H NMR spectrum of mpd 3 76
2.12.5.7 1H NMR spectrum of mpd 4 77
2.12.5.8 1H NMR spectrum of mpd 6 78
2.12.5.9 1H NMR spectrum of BI-02 79
2.12.5.10 1H NMR spectrum of BI-03 80
2.12.5.11 Mass spectrum of mpd 1 81
2.12.5.12 Mass spectrum of mpd 3 82
2.12.5.13 Mass spectrum of mpd 4 83
2.12.5.14 Mass spectrum of mpd 6 84
2.12.5.15 Mass spectrum of BI-05 85
2.12.5.16 IR spectrum of mpd 4 86
2.12.5.17 IR spectrum of mpd 5 87
2.13 Biological activity 88
2.14 References 115

Chapter 3 Part A **Synthesis, characterization and biological activity of pyrimidine-2-thione and pyrimidin-2-one derivatives by Biginelli reaction** 120
3.1 Biginelli Reaction 121
3.2 Mechanistic Studies of Biginelli Reaction 122
3.3 Alternative synthetic routes 123
3.3.1 Catalysts 123
3.3.2 Solid Phase Synthesis 133
3.3.3 Microwave assisted synthesis 136
3.3.4 Ionic liquid 138
3.4 Biologically active dihydropyrimidones 139
3.5 Current work 145
3.6 Reaction Schemes 146
3.6.1 Synthesis of pyrimidine-2-thione and pyrimidin-2-one 146
3.7 Experimental 146
3.8 Physical data 147
3.8.1 Physical data of 4-(substitutedphenyl)-1,3,4,5-tetrahydro-substitutedindeno[1,2-d]pyrimidine-2-thione or pyrimidin-2-one [compounds 4a-l] 147
3.9 Spectral discussion 148
3.9.1 Mass spectral study 148
3.9.2 IR spectral study 149
3.9.3 1H NMR spectral study 149
3.9.4 Elemental analysis 149
3.9.5 Spectral data of synthesized compounds 149
3.9.5.1 1H NMR spectrum of 4d 153

3.9.5.2 1H NMR spectrum of 4b 155
3.9.5.3 Mass Spectrum of 4d 156
3.9.5.4 Mass spectrum of 4k 157
3.9.5.5 Mass spectrum of 4l 158
3.9.5.6 IR spectrum of 4c 159
3.9.5.7 IR spectrum of 4d 160
3.10 Biological activity 161
3.10.1 Antimicrobial activity of compounds 4a-l 166
3.11 References 169
Chapter 3 Part B Synthesis, characterization and biological activity of dihydro-1H-indeno[1,2-d]pyrimidine derivatives 173
3.12 S-Alkylation Reaction 174
3.13 Biologically active S-alkylated dihydropyrimidones 179
3.13.1 Antihypertensive agents 179
3.13.2 Antitumor activity 180
3.13.3 Miscellaneous activities 181
3.14 Current work 181
3.15 Reaction Scheme 182
3.15.1 Synthesis of dihydro-1H-indeno[1,2-d]pyrimidine derivatives 182
3.16 Experimental 182
3.17 Physical data 183
3.17.1 Physical data of dihydro-1H-indeno[1,2-d]pyrimidine derivatives 183
3.18 Spectral discussion 184
3.18.1 Mass spectral study 184
3.18.2 IR spectral study 184
3.18.3 1H NMR spectral study 184
3.18.4 Elemental analysis 185
3.18.5 Spectral data of synthesized compounds (5 a-j) 185
3.18.5.1 1H NMR spectrum of 5a 187
3.18.5.2 1H NMR spectrum of 5b 189
3.18.5.3 Mass Spectrum of 5c 190
3.18.5.4 Mass Spectrum of 5e 191
3.18.5.5 Mass Spectrum of 5j 192
3.18.5.6 IR spectrum of 5a 193
3.18.5.7 IR spectrum of 5b 194
3.19 Biological activity 195
3.19.1 Antimicrobial activity of compounds 5a-j 200
3.20 References 203

Chapter 4 Synthesis, characterization and biological activity of 2-thioxo-2,3,4,6,7,8-haxahydro-1H-quinazolin-5-one and hydrazine-4,6,7,8-tetrahydro-3H-quinazolin-5-one derivatives 205
4.1 Introduction 206
4.2 History 210

4.3 Chemical Properties of Quinazolines 211
  4.3.1 Hydrolysis, Oxidation, and Reduction 211
  4.3.2 Reduction 211
4.4 Nucleophilic and Electrophilic Substitution Reactions 212
  4.4.1 Electrophilic Substitution Reaction of Quinazoline 212
  4.4.2 Alkylation Reactions 213
  4.4.3 Addition Reactions 213
4.5 Synthesis of Quinazoline Compounds 213
  4.5.1 Niementowski's Synthesis 213
  4.5.2 Grimmel, Guinther, and Morgan's Synthesis 214
  4.5.3 From Isatoic Anhydride 214
  4.5.4 From 3,1,4-Benoxazones (Acylanthranils) and Amines 215
  4.5.5 From Ethyl 2-Acetamido-5-nitrobenzoate 215
  4.5.6 Sen and Ray's Synthesis 215
4.6 Methods for the Synthesis of Quinazoline and Quinazolinone Derivatives (Benzoylene Urea) 216
  4.6.1 From Anthranilic Acid and Urea 216
  4.6.2 From o-Ureidobenzoic Acid 216
  4.6.3 From o-Ethoxy Carbonyl amino benzoic Esters or Amides 217
  4.6.4 From Phthalic Acid Derivatives 217
  4.6.5 From Isatins 217
  4.6.6 From 2-Aminobenzylamine 218
  4.6.7 From 2-Azido-4-chlorobenzoic Acid 218
4.7 Biological Importance of Quinazoline Derivatives 219
  4.7.1 Quinazolinones as Anticancer Activity 220
  4.7.2 Quinazolinones as Antibacterial Activity 229
  4.7.3 Quinazolinones as Antifungal Activity 232
  4.7.4 Antitubercular Activity 232
  4.7.5 Quinazoline as Antiviral Agents 233
  4.7.6 Quinazolinones as Antimutagenic Activity 234
  4.7.7 Quinazolinones as Anticoccidial Activity 234
  4.7.8 Anti-Inflammatory and Analgesics Agents 235
  4.7.9 Quinazoline as Antidepressant and Anticonvulsant 238
  4.7.10 Quinazolinones as Antimalarial Agents 241
  4.7.11 Quinazolinones as Antioxidant Activity 242
  4.7.12 Antileishmanial Agents 243
  4.7.13 Quinazoline as Neuroprotective Agents 244
  4.7.14 Quinazoline as Antiobesity Agents 244
  4.7.15 Antihypertensive Agents 244
  4.7.16 Anti-H1-Antihistaminic Agents 245
  4.7.17 Quinazoline as Antiprotozoan Agents 245
4.8 Current work 246
4.9 Reaction Scheme 247
4.10 Experimental 248
4.11 Physical data 248
4.12 Spectral discussion 249
  4.12.1 Mass spectral study 249

4.12.2 IR spectral study 250
4.12.3 1H NMR spectral study 250
4.12.4 Elemental analysis 251
4.12.5 Spectral data of synthesized compounds (2a-h and 3 a-j) 251
4.12.5.1 1H NMR spectrum of 3a 256
4.12.5.2 Carbon NMR spectrum of 3a 258
4.12.5.3 1H NMR spectrum of 3i 260
4.12.5.4 Mass spectrum of 3a 261
4.12.5.5 IR spectrum of 3a 262
4.12.5.6 IR spectrum of 3c 263
4.13 Biological activity 264
4.13.1 Antimicrobial activity of compounds 2a-h and 3a-j 269
4.14 References 272

Chapter 5 Summary and conclusion 279